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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,215	05/17/2001	Peter Huub Gerard Maria Kirchholtes	D/98409 US	7592

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TRASKBRITT, P.C.
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,215	KIRCHHOLTES ET AL.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6 and 22-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6 and 22-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/8/04,5/17/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on May 17, 2004 wherein Claims 1-3, 7-20 are cancelled; claims 4-6 have been amended; claims 21-29 are newly submitted.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Since applicant has two presented claims numbered 24, the claims herein have been renumbered in accordance with Rule 126, and the dependency of renumbered dependent claims has been completely changed as well.

Thus, the new claims herein are now numbered 22-29 instead of 22-28.Currently, claims 4-6 and 21-29 are pending in this application.

Claims 4-6 and 21-29 as amended now are examined on the merits herein.

The Parallel Litigation / European Patent Office Oppositions (see Applicant's remarks filed May 17, 2004 at page 4) and supplemental IDS filed March 8, 2004, May 17, 2004, and May 21, 2004 are acknowledged.

The following is new rejection(s) necessitated by Applicant's amendment filed May 17, 2004, wherein the original claims 1-3, 7-20 are cancelled and new

claims have been added. Therefore, all rejections of record in the previous Office Action February 2, 2004 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 24-25, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites "tibolone of Org OM38 as an impurity". There is insufficient antecedent basis for this limitation, since the independent claim 4 which claim 21 is dependent from does not recite "tibolone of Org OM38 as an impurity".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-6 and 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sas et al. (EP 389035 A1, of record) and Van Vliet et al. (of record).

Sas et al. teaches a process for preparing the high pure (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one comprising aging crystal of (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one including the step, seeding crystals in the presence of water for one hour. Sas et al. also teaches the steps of the process herein such as pouring out the solution in water with small amount of pyridine which makes the solution slightly alkaline and washing the crystals with water and small amount of pyridine which makes the solution slightly alkaline. See Examples 1-4.

Note that the recitation "*less than* 0.5%, 0.25%, or 0.1% by weight relative to tibolone of Org OM38 as an impurity after drying" in the instant claim 21 is seen to merely limit the claims to any amount less than 0.5%, 0.25%, or 0.1% by weight including 0%. Thus, the composition of Sas prepared therein comprising 0% by weight of impurity of tibolone of Org OM38 meets this limitation.

Vliet et al. teaches the last step of synthesis of (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one: reacting (7α, 7α)-3,3-dimthoxy-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one in an organic solvent with aqueous oxalic acid (a weak acidic aqueous solution). See page 112 the last line of the 2nd paragraph to the first line of the 1st paragraph. Vliet et al. also teaches that the instant impurity of (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-**4-en**-20-yn-3-one, Compound 21, is present with the desired product, (7α,

7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one, Compound 4, in a composition with less than 1%, isolated and identified by ^{1}H NMR, IR and UV (see page 113 the 1st paragraph of the right column).

The prior art does not expressly disclose that the step of the process herein for aging crystals lasts for at least 24 hours or 3-6 days and pouring out the solution in slight alkaline water and washing the crystals with slight alkaline water.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to optimize the time period for aging crystals to at least 24 hours or 3-6 days and to pour out the solution in slight alkaline water and to wash the crystals with slight alkaline water.

One having ordinary skill in the art at the time the invention was made would have been motivated to optimize the time period for aging crystals to at least 24 hours or 3-6 days because the optimization of the time period for aging crystals to longer period of time in order to obtain more desirable crystals, e.g. highly pure or desired polymorphous forms, is considered well within the skill of artisan. The book "Modern Experimental Organic Chemistry" by Roberts et al. (PTO-1449 March 31, 2003) clearly supports the examiner's position herein since crystallization and recrystallization by optimizing variables, e.g., time, solvents, and temperature, are well within the skill of artisan (see page 67-75).

Additionally, one having ordinary skill in the art at the time the invention was made would have been motivated to pour out the solution in slight alkaline water and to wash the crystals with slight alkaline water. As discussed above, the

steps including pouring out the solution in slight alkaline water and washing the crystals with slight alkaline water are a **conventional** to a skilled artisan, involving merely routine skill in the art, especially Sas has disclosed the steps herein, pouring out the solution in water with small amount of pyridine which makes the solution slightly alkaline and washing the crystals with water and small amount of pyridine which makes the solution slightly alkaline. Vliet et al. also teaches that an organic solvent with aqueous oxalic acid (a weak acidic aqueous solution) was utilized in the last step of synthesis of (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one while the instant purity compound is known to be present therein, one of ordinary skill in the art would reasonably employ slight alkaline water to neutralize the final product mixture in order to purify the desired product.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed on May 17, 2004 with respect to this rejection of claims 4-6 made under 35 U.S.C. 103(a) in the previous Office Action have been fully considered and but are not deemed persuasive to remove the rejection.

Applicant asserts that "for obviousness, specifically admonished by the MPEP 2143 (2100-126):

FACT THAT THE CLAIMED INVENTION IS WITHIN

THE CAPABILITIES OF ONE OF ORDINARY SKILL IN THE ART IS NOT SUFFICIENT **BY ITSELF** TO ESTABLISH PRIMA FACIE OBVIOUSNESS" (emphasis added, see Applicant's remarks at 6).

Applicant's attention is directed to the phrase, "by itself", i.e., in the scenario, absent prior art reference cited in the obviousness rejection, but rejecting a claim(s) with the particular limitation(s) by solely relying on the capability of one of ordinary skill in the art, which would be specifically admonished by the MPEP 2143.

In this case, as discussed above, the cited prior art Sas et al. and Vliet et al. clearly teaches a process for preparing the high pure (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one comprising aging crystal of (7α, 7α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one including the steps as instantly claimed, pouring out the solution in water with small amount of pyridine which makes the solution slightly alkaline and washing the crystals with water and small amount of pyridine which makes the solution slightly alkaline, and seeding crystals in the presence of water for one hour,

The text book "Modern Experimental Organic Chemistry" by Roberts et al. (PTO-1449 March 31, 2003) clearly teaches the old and well known techniques in chemistry, crystallization and recrystallization by optimizing variables, e.g., time, solvents, and temperature (see page 67-75).

It must be recognized that any judgment on obviousness takes into account knowledge which was available and within the level of ordinary skill at

the time the claimed invention was made. In re McLaughlin , 170 USPQ 209 (CCPA 1971). See MPEP 2145. Note that arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135,139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). In this case, clear and convincing evidence of nonobviousness or unexpected results for the claimed process herein over the prior art is not seen.

Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

For the above stated reasons, the claimed invention is clearly obvious in view of the prior art. Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory

period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
August 27, 2004

SHAOJIA ANNA JIANG
PATENT EXAMINER
9/7/04